Abstract

Dengue is an emerging public health concern not only in Asian subcontinent but also in remote areas of world secondary to increase in number of mosquitoes, congested living facilities & lack of personal hygiene. Annually, morbidity and mortality secondary to dengue has created significant public health concerns from a socio-economic standpoint which requires increased awareness to general public. In this paper, we discuss a case of a patient who was diagnosed with dengue in urban India. Here we elaborate upon various systemic manifestations of dengue fever and also demonstrate the progression of this patient throughout the time course in hospital. In addition, we also elaborate on an interesting public health model that has been used to risk stratify areas affected with Dengue.

Keywords: Emerging, Subcontinent, Hygiene, Dengue, Public Health.

Introduction

Dengue fever is a multisystem disorder caused due to infection by Dengue virus which is a ssRNA virus belonging to a Flaviviridae family (Rodenhuis et. al, 2010; WHO 2009). Many different serotypes of this virus have been recognized of which NS-1 is the most common and lethal (Rodenhuis et. al, 2010; WHO 2009). Clinical presentation of Dengue can vary from being asymptomatic to very severe presenting as fever, joint pain, muscle aches, skin rash characterized by erythema and warmth, narrow pulse pressure and delayed capillary refill. Minority of patients end up progressing to a more severe form of shock or hemorrhagic fever which includes additional hematological manifestations like pancytopenia.
bleeding and severe hypotension secondary to septic shock (WHO 2009).

Transmission of virus occurs via vector (mosquitoes) Aedes Aegypti which are harbored in increased number in stagnant water. After infection, multiple different immunological factors get activated within the host. Due to increased viral titers there is endothelial dysfunction, increased mononuclear cell replication in Langerhans cells and splenic macrophages, stimulation of cross reaction of T cells leading to bone marrow suppression and coaguloapathies (Martina et. al, 2009).

It is also possible that local vascular beds can be a target of dengue virus which can lead to increased endothelial cell retraction leading to leakage of vascular contents into interstitial fluid leading to presentation very similar toxic shock syndrome which presents with hypotension, flushing and severe hemodynamic instability which required aggressive fluid resuscitation (Martina et. al, 2009).

**Case Details (Patient profile, interventions and outcome)**

Patient is a 40 year old male who was brought to ED due to progressive worsening joint pain, fever and a red rash on different parts of his body since 2 weeks prior to admission along with chills, nausea and non-bloody, non-bilious vomiting. Patient denies any other associated symptoms like visual changes, dizziness, chest pain or shortness of breath. No sick contacts in family or any recent travel. Pa-

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**Figure 1: LISA Model- Helps is assessment of significant risk based on three temporal indices namely (1) Frequency, (2) Duration and (3) Severity of Dengue Symptoms**

Patient’s past medical and surgical history is non-significant. No known drug allergies. No smoking, drinking or illicit drug use. Denies taking any medications. Patient works as a project manager in a local construction work site in India. Review of systems as per history of present illness mentioned above. On physical exam, patient had mild diffuse abdominal tenderness in all 4 quadrants, without any rebound tenderness; (+) Hepatomegaly 2 to 3 cm below the right costal margin, (+) Splenomegaly, (+) Ascites. In addition, there is non-blanching rash with red discoloration in the periumbilical area and dorsal aspect of the forearm and lower extremities bilaterally. Capillary refill time was 4 to 5 seconds. In addition, on musculoskeletal exam, there was pain upon flexion & extension of PIP, DIP, knee, hip and elbow joints. Consequently, patient was admitted to the hospital and fluid resuscitation was initiated with 0.9% NS. Basic labs were ordered including complete blood count, complete metabolite panel and liver function tests. Significant results on blood work demonstrated pancytopenia with platelet count 16000, Hemoglobin: 9.7 and WBC: 2800. Chest X-ray demonstrated bilateral pleural effusion. Abdominal ultrasound confirmed hepatosplenomegaly. Dengue was suspected and NS-1 antigen was ordered which was positive; IgG was positive and IgM was positive. This confirmed that patient had a primary infection with dengue virus. Immediately, patient was placed on complete bed rest, given 3 packs of standard platelet rich plasma (PRP) every day to address thrombocytopenia and placed on IV hydration 0.9% NS 100ml/hour. In addition, broad spectrum antibiotics: Cefoperazon + sulfa-bactam 1.5gm IV twice a day (BID), Gentamycin 80 mg IV BID and Moxifloxacin 400 mg IV BID, were initiated to prevent bacterial superinfection. After 14 days of hospitalization patient returned to his baseline and was discharged.

**Discussion**

Dengue is a major public health issue globally. It has been found that, "...estimated that about 2.5 billion individuals, a staggering 40% of the world population, inhabit areas where there is a risk of transmission of DF (Dengue Fever) and that the disease burden has increased at least fourfold in the last three decades. Modelling also suggests that approximately 50–100 million human infections occur annually, of which about 500,000 are DHF (Dengue Hemorrhagic Fever)". (Guzman et al, 2010). Prevention is extremely important via early detection and reducing rate of transmission. Best prevention can be achieved by avoiding travel in endemic areas during monsoon when Dengue is the most prevalent. Further reduction of transmission can occur via use of mosquito

| Table 1: Diagnostic differences between Zika, Chikungunya and Dengue |
|------------------|------------|-------------|-----------------|------------------|
|                  | Fever     | Rash | Conjunctivitis | Joint Pain (Arthralgia/Myalgia) | Sign of Sepsis (Haemorrhage/ Shock) |
| Zika             | +         |      |                |                                |                                |
| Chikungunya      | +         |      |                |                                |                                |
| Dengue           | +         |      |                |                                | +                               |
sprays multiple times a day in house to prevent harboring, stay in a well ventilated cold environment and wear mosquito repellent protection on skin with topical emollients like permethrin.

Two common modes of transmission of Dengue are epidemic and hyper-endemic dengue (Tukasan et. al, 2017). In hyperendemic dengue, disease and vectors are always present in local area and viral strain circulates either seasonally or all year around in humid environment which leads to more infections (Tukasan et. al, 2017). In contrast, epidemic dengue is an introduction of new strain brought on by an isolated transmission from area outside of infection which starts an infectious cycle amongst hosts (Tukasan et. al, 2017). We believe this patient to be affected due to hyperendemic dengue. However, due to increase global immigration, it is possible that dengue strains can become a widespread epidemic or even a pandemic. In terms of diagnosis NS-1 antigen test has been used extensively to assess the index of suspicion of Dengue fever. Study by Paravnitane et. al, demonstrated rapid NS-1 antigen detection test to be extremely efficient in outpatient setting at bedside and had comparable sensitivity and specificity.

Figure 2 and 3: The resolution of pancytopenia as the hospital stay progresses. Improvement in platelet count, hemoglobin and WBC count from HD 1 thru HD 14.
to NS-1 antigen capture ELISA (Murray et al., 2013). In addition, presence of NS-1 antigen is extremely important in predicting high clinical severity of disease. Recently, it has been found that NS-1 antigen induces pathogenesis by induction of interleukin 10. (Adikari et al., 2016).

In addition, the symptom of “fever” has been proven to be the most significant predictor in terms of diagnosis for patients with Dengue infection and stratifying patients in low vs high risk. For instance, in a recent retrospective study “Disease classification was found to associate significantly with both fever and time to treatment (both P < 0.001). Non-febrile patients were nearly four-fold more likely to exhibit “dengue without warning signs” than “severe dengue” (odds ratio [OR] = 3.74; 95% confidence interval [CI]: 3.20–4.36)” (Hafeez et al., 2017). In the same study interestingly, “Patients who received treatment within 7 days were twice as likely to have ‘dengue without warning signs’ as opposed to ‘severe dengue’ when compared to those who waited >7 days (OR = 2.23; 95% CI: 1.78–2.80)” (Hafeez et al., 2017). So it is important for clinicians to have a high index of suspicion for Dengue infection if a patient presents to them with a recent travel history from a dengue affected endemic area. Other factors that determine prognosis should include old age and low oxygen saturation and other including septic shock, sepsis and pneumonia.

From a public health standpoint, many different models have been developed that help in ensuring better preventative measure. One of them being LISA (Local Index of Spatial Autocorrelation) which takes into consideration many demographic factors for developing a TI (Temporal Index): (1) Frequency index, (2) duration index to assess severity of epidemics and (3) severity index (Teparrukkul et al, 2017). This model has enabled public health researchers to divide the dengue affected areas into 5 major subtypes: demonstrated in Figure 1.

Biggest challenge with this patient was addressing thrombocytopenia and ensure its resolution over time with treatment. As we can see in the figures II and III, it took 14 days of hospital stay for this patient to get back to baseline hematological status. Resolution and improved bone marrow response can be monitored by serial physical examinations to look for elimination of rash (Figure I), ascites and joint pain. In addition, it is important to rule out disorders like chikungunya which has similar presentation but has the hallmark of bone breaking fever without pancytopenia. With growing incidence of Zika virus in US (which is also transmitted by A. Aegypti), Dengue and Chikungunya should always be considered in clinical decision making.

Conclusion

In summary, we have presented a case report of a patient who was diagnosed with Dengue based fever and successfully recovered in 2 weeks secondary to aggressive hydration therapy and preventative measures. In addition, we have also discussed LISA model that can be used on a global scale to stratify areas depending on the level of risks that can enable public health officials to prioritize areas of treatment. And finally, we have also elaborated on how one can clinically diagnose Dengue based on physical exam (with a characteristic rash) and blood work.

Learning Points

♦ Elaborate on clinical presentation of patients with Dengue fever.
♦ Discuss clinical progression and treatment options of a patient with Dengue.
♦ Discuss an interesting clinical model used to stratify areas affected with dengue.

Ethical Information

Patient consent was obtained in order to acquire images for educational purposes and patient privacy was preserved through
the case study.

**Conflict of Interest**
The authors declared no conflicts of interest with respect to the research, authorship and/or publication of this

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Arrows in image above demonstrate a characteristic rash with red discoloration on the upper & lower extremities along with abdomen. Rash is used clinically to ensure remission of patient from dengue fever after initiation of treatment.
References


